Total artificial heart in two-staged cardiac transplantation

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Since the first clinical cardiac transplantations were made more than a decade ago,[1-3] a major limitation of the technique has been that it was available primarily for elective use only and not on an emergency basis. To overcome this obstacle, in 1969, we proposed a two-staged cardiac transplantation with a total artificial heart (TAH) as the first stage to maintain the patient's life until preparations could be made for cardiac allografting.[4] In that report, we described a 47-year-old man whose life was sustained for 64 hours with a TAH and another 32 hours by a cardiac allograft, thus indicating that the TAH had clinical applicability. The major complications described were early hemolysis, probably due to the fabric (Dacron) internal lining of the ventricle, and marginal function of the pumping chambers caused by the incompetence of Wada-Cutter hingeless valves.

During the years since 1969, investigations in the Cullen Cardiovascular Research Laboratories of the Texas Heart Institute have continued under separate programs for ventricular assist devices[5-7] and for the total artificial heart.[8,9] Extensive *in vitro* and *in vivo* tests of the TAH culminated recently in the development of a prosthesis considered suitable for clinical application.

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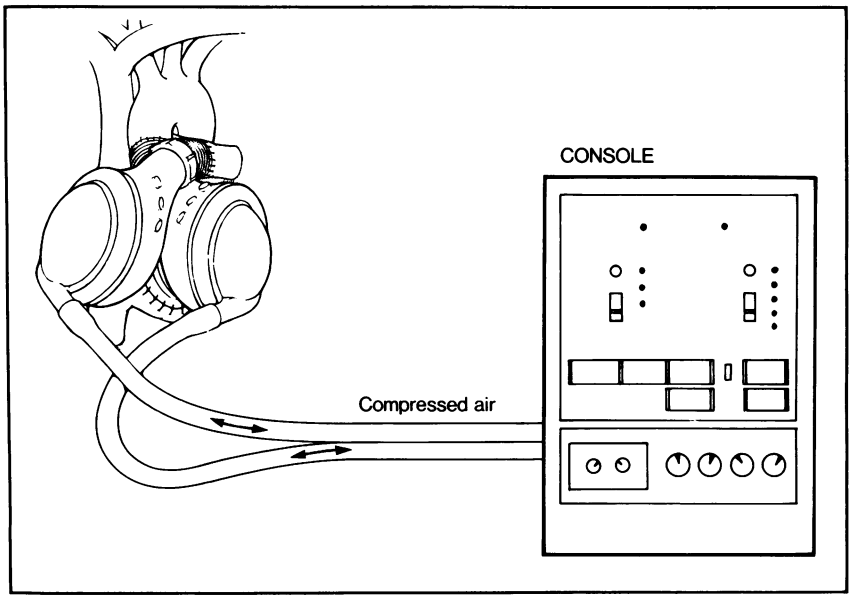

Fig. 1 Diagram showing the orthotopic placement of the total artificial heart.

Description of the Device (Total Artificial Heart)

The implantable *prosthesis,* the Akutsu Model III, Series 3 TAH, combines two pneumatically-powered (compressed air), double-chambered pumps by using the principle of a reciprocating hemispherical diaphragm (Fig. 1). The seamless one-piece pumping chambers are fabricated from Avcothane 51 (Avco Everett Corporation*). Björk-Shiley convexo-concave disc valves** are incorporated in the inflow (29 mm) and outflow (25 mm) ports of the pumping chambers. The valves were selected because of their large orifice area, low impedance to blood flow, and low clinical incidence of thromboembolic complications. The prosthetic ventricles are attached to the atria and great vessels by flexible inflow and outflow conduits with detachable quick-connectors. The atrial connections are fabricated from silastic, with a velour cuff; the pulmonary and aortic connectors are fabricated from 25 mm low porosity Dacron grafts. Before attaching the arterial connectors to the aorta and pulmonary arteries, they are preclotted with autologous plasma and exposed to auto-

*Available from Kontron Cardiovascular, Inc. (Formerly Avco Everett Corp.), 9 Plymouth Street, Everett, Massachusetts 02149.

**Shiley Inc., 17600 Gillette Avenue, Irvine, California 92714.

claving for 5 minutes to further reduce the porosity.[10] The orthotopically-positioned pumps are connected to an external control console with Dacron velour-covered Tygon tubing (inner diameter, 10 mm). The drive tubes are tunneled caudad and emerge from the left and right hypochondrium.

The drive *console* consists of three basic systems: the pneumatic drive system, an electrical monitoring/control system, and an electrical power system. The pneumatic system simultaneously supplies a separate measured pressure and measured vacuum to each ventricle. The supply side of each pressure and vacuum parameter is controlled and monitored. Additional dynamic monitoring of ventricular driveline pressures is displayed on a long-persistence, dual-trace oscilloscope. Redundant (parallel), low-pressure drop solenoid valves are used to control the alternate application of pressure and vacuum to each ventricle. The heart rate and systolic duration are the primary functions of the electrical control system and are common for both ventricles. The monitoring system provides digital read-outs of pressure and vacuum supplies, as well as standard and emergency power supply status.

The power supply system consists of two independent sources of electrical power. A standard AC to DC power supply is the primary power source. A battery-powered emergency power supply will automatically engage upon AC power failure.

The drive console parameters used during artificial heart pumping may be varied according to need. For the average human support, they are:

	Drive Pressure (mm Hg)	Filling Pressure (mm Hg)	Rate (B/min)	Ejection Duration (msec)
Left Heart	100-165	-5 to -25	45-90	250-310
Right Heart	40-70	-5 to -25	45-90	250-310

Case Report

A 36-year-old man was admitted to this hospital on July 20, 1981, with ischemic myocardial insufficiency for consideration of myocardial revascularization by means of saphenous vein aortocoronary bypass grafting. His symptoms of angina pectoris and dyspnea on exertion began 1 year prior to admission. Cardiac catheterization had been performed first in Holland in 1980, and the results were sent here with the patient in January 1981 for an opinion regarding the need for revascularization. After repeat cardiac catheterization and selective coronary arteriography that revealed the diffuse nature of coronary disease and the peripheral location of some of the arterial lesions, it was recommended that a trial of more intensive medical management would be appropriate. He was discharged on a regimen of Isordil, 20 mg qid;

Inderal (propranolol), 60 mg qid, with aspirin and Persantine. A low fat diet was also recommended for control of hyperlipidemia.

On the current admission, he returned with complaints of chest pain of increasing frequency and duration. He had retired from work because of the severity of his symptoms. Angina could be precipitated with 200 meters of exercise and relieved with nitroglycerin. His medications on admission included Inderal, 40 mg tid; Persantine, 75 mg tid; Adalat (Nifedipine), 10 mg tid; Cedocard (sorbide nitrate), 20 mg tid; Rhonal (an aspirin derivative), 500 mg bid; Seresta (Serax, a valium-like medication), 10 mg tid; and Nitrobaat (nitroglycerine), 1 mg prn. His clinical history revealed that his father had a long history of heart disease and died of myocardial infarction at the age of 56.

Physical examination disclosed a well-developed, well-nourished but anxious 36-year-old man in no acute distress. Blood pressure was 110/80. The pulse rate was 78 B/min and regular. There was a slight precordial heave over the left chest. The PMI was palpable in the fifth intercostal space, just lateral to the mid-clavicular line. All peripheral pulses were present without bruits. The abdomen was nontender, without masses or organomegaly. The neurologic, genitourinary, musculoskeletal and rectal examinations were within normal limits.

The electrocardiogram and chest film were not abnormal. The white count was 10,300 with a normal differential; the hemoglobin concentration was 15.2 mg%, and the hematocrit was 43.3%. The prothrombin time was 12 seconds with a control of 12.5, and the serum electrolytes, creatine and blood urea nitrogen were within normal limits.

Review of the coronary artery arteriography revealed a 50% lesion of the distal one-third of the right coronary artery, a 75% occlusive lesion of the post-diagonal left anterior descending, a 75% occlusive lesion of the proximal ramus medialis, and total occlusion of its bifurcation, with near total occlusion of the first obtuse marginal branch of the circumflex in the second obtuse marginal position. Coronary artery occlusive disease had progressed, and operation was recommended. The chronology of subsequent events is summarized in Table I.

Myocardial Revascularization

On July 23, 1981, operation was undertaken with temporary cardiopulmonary bypass (CPB), moderate systemic hypothermia (30°C), topical cardiac hypothermia and infusion of cardioplegic solution in the aortic root. A triple reversed saphenous vein aortocoronary bypass procedure was effected by placing grafts into the posterior descending branch of the right coronary artery, the left anterior descending artery, and the ramus medialis of the circumflex artery. The aortic cross-clamp time was 45 minutes.

TABLE I. Chronology of Events

Date	Time	Procedure	Duration (hrs)
7/23/81	7:30 A.M.	Triple vessel aortocoronary bypassing	1.5
7/23/81	10:00 A.M.	Intraaortic balloon insertion	7
7/23/81	5:00 P.M.	Intraaortic balloon removal; Implantation of total artificial heart	54
7/24/81	7:45 P.M.	Extracorporeal membrane oxygenerator (ECMO) utilization	27
7/24/81	10:30 P.M.	Cardiac transplantation and termination of ECMO	178
8/2/81	8:00 A.M.	Patient expired 7½ days post-transplantation	

Insertion of the Intraaortic Balloon Pump (IABP)

Following release of the cross-clamp, he could not be weaned from cardiopulmonary bypass despite intravenous Digoxin, Isoproterenol and Epinephrine. Therefore, a 30 ml intraaortic balloon pump (IABP) and cable were inserted via the left common femoral artery, and weaning from CPB was finally effected after 1 hour and 35 minutes of support. The patient was returned to the intensive care unit with continued IABP support. During the next two hours, he progressed in our circulatory support hemodynamic classification from Class C through B to A.[7,11] The peak arterial systolic pressure was 110 mm Hg without vasopressors. The electrocardiogram, however, revealed a newly-developing left bundle branch block pattern, inferolateral Q waves, and S-T changes laterally, indicative of perioperative inferolateral myocardial infarction.

Clinical Course

Three hours after arrival in the ICU, the QRS complex suddenly widened and the blood pressure fell to less than 50 mm Hg systolic. External cardiac compression was ineffective in maintaining cardiac output, so the sternotomy incision was opened and manual massage was begun. No intrapericardial bleeding was encountered, and the three vein grafts were patent. Resuscitative medications included dopamine, calcium chloride, Epinephrine, Lidocaine, bretylium tosylate, and Levophed. Multiple electric countershocks were applied to arrest ventricular fibrillation but were not effective.

Partial Cardiopulmonary Bypass

The patient was returned to the operating room during continued internal cardiac massage. After 45 minutes of massage, partial cardiopulmonary bypass was begun by inserting cannulae into the right common femoral artery and vein. At flows of 2500 ml/min, the pupils became reactive, and there was evidence of electroencephalographic activity. Multiple attempts at weaning the patient from partial cardiopulmonary bypass were unsuccessful despite reinstituted IABP support. Because of the presence of severe biventricular failure and a flaccid, motionless heart, the only recourse, in our opinion, was to utilize a total artificial heart. At this point, the desperate condition of the patient was explained to his wife, who gave verbal and written consent for the use of the total artificial heart.

Implantation of the Total Artificial Heart (TAH)

The superior vena cava was cannulated and total cardiopulmonary bypass was employed. The heart was excised and an Akutsu Model III, Series 3, TAH was implanted (Figs. 1 and 2). The separate attachment rings for the left and right atria, the aorta, and the pulmonary artery were sutured with 3-0 polypropylene monofilament suture in a continuous fashion. The left ventricle was attached first to the snap-on connection on the left atrium and then to the aorta. The right ventricle was attached to the right atrial and pulmonary artery cuffs. The connections were secured with a heavy No. 2 braided polyester suture ligature incorporated in the sleeve. Additional interrupted sutures were used between the velour fabric on the ventricles and the cardiac attachment rings. No bleeding occurred from the lines of attachment. The drive tubes were passed through the abdominal wall to emerge from the right and left hypochondria.

On July 23, 1981, at 5:45 PM, total artificial heart pumping was initiated at 45 BPM and increased through 60 BPM to 80 BPM as cardiopulmonary bypass was discontinued after a total of 100 minutes.

Despite reversal of the heparin by Protamine sulfate, diffuse bleeding was encountered. Blood derivatives, including fresh frozen plasma, platelets, and cryoprecipitate were administered without apparent effect. The thoracic incision was partially closed by approximating only the skin and subcutaneous tissues and not the sternum.[12] He was returned to the ICU with the circulation totally maintained by the total artificial heart.

Clinical Course

Occasional adjustments of the console parameters were necessary to maintain atrial pressures in the range of 10 to 20 mm Hg. The maxi-

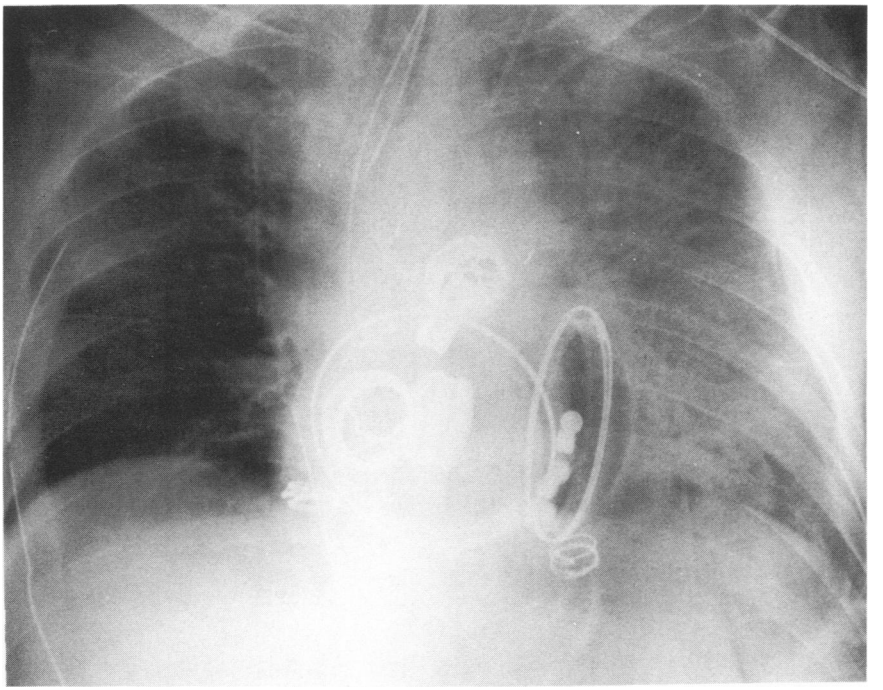

Fig. 2 Roentgenogram of the chest showing the total artificial heart in situ 6 hours after implantation. Note that the lungs are clear.

mum right and left ventricular stroke volumes of the TAH were 80 ml, depending on venous return. The prosthetic-generated cardiac outputs ranged up to 3.5 to 4.0 L/min. Good hemodynamic and hematologic responses were obtained (Fig. 3, Table II). The coagulopathy was difficult to control, but after intensive treatment with blood derivatives, particularly platelet infusions and cryoprecipitate, bleeding ceased approximately 24 hours later (Table II).

Renal function was adequate initially, with urinary output averaging 40 to 50 cc/min, but oliguria progressed to anuria 36 hours after implantation of the TAH.

Pulmonary function posed a problem of major concern. Roentgenograms of the chest initially revealed normal radiolucency of both lungs (Fig. 2). However, within 8 hours after implanting the TAH, the left lung appeared congested, and the right lung was abnormally radiolucent.

Approximately 24 hours after implanting the TAH, the arterial PO_2 had fallen to 20 mm Hg, and the arterial pCO_2 had risen to 60 mm Hg. For this reason, extracorporeal membrane oxygenation (ECMO) was initiated at 7:45 PM on July 24 and continued for approximately 27 hours, until 10:45 PM on July 25 (Fig. 4). The membrane oxygenator used was

TABLE II. Formed Element and Coagulation Profiles During Total Artificial Heart Support of the Circulation

Event Date/Time		Hours Post TAH Implant	RBC ($\times 10^6$)	Hgb (gm%)	Hct (%)	Plasma Hgb (mg.%)	PT (sec)	PTT (sec)	Fibrin. (mg/dl)	Platelets (/cmm)	Rept.* (sec)	Comments
7/22		preop	4.79	15.2	43.3		12					Preoperative data
7/23												
TAH	5:45P	0.5	3.01	9.4	27.8	252	>110	>110	38	33,000	48	On cardiopulmonary bypass Patient heparinized
	7:45P	2.5	4.01	12.6	36.7		16	37	185	169,000		Off cardiopulmonary bypass 10 units cryoprecipitate & 10 units platelets given
	9:30P	4.5	3.75	11.7	34.4	185	16	41	160	111,000		
	11:30P	6.5	3.75	11.6	34.2	13.0	16	44	160	110,000		
7/24	1:30A	8.5	3.5	13.4	40.5	92.0	16	57	130	77,000		10 units cryoprecipitate & 10 units platelets given
	4:00A	11	3.46	10.6	31.4	49.3	15	47	185	100,000		
	6:00A	13	3.5	11.0	32.2		16	51	160	80,000		10 units cryoprecipitate given
	7:30A	14.5	3.5	13.8	38.4	13.4	14	43	250	74,000		
	11:00A	18	3.6	13.2	39.5	14.0	14	35	225	90,000		
	3:00P	22	3.5	11.5	33.9		15	36	225	85,000		
	4:45P	24					16	46	195	68,000		

Patient Placed on Extracorporeal Membrane Oxygenator (ECMO)

ECMO	7:45P	27	4.45	13.8	38.4	11.8	16	50	185	53,000	Started on ECMO at 7:45pm Heparinized. Platelets maintained at 50,000
	8:15P	27.5	3.66	11.2	37.0	29.0	35	>110	123	38,000	16 8 units platelets given
	10:30P	30	3.64	11.0	31.4	33.0	19	>110	130	61,000	21 8 units platelets given
7/25	12:30A	32	3.54	11.3	30.3	25.2			120	63,000	19
	3:00A	34.5	3.46	10.4	28.8	25.2			135	50,000	21
	5:00A	36.5	3.35	10.1	28.1	27.0			145	44,000	23 10 units platelets given
	7:30A	39	3.87	11.6	33.3	42.5			150	75,000	24
	10:00A	41.5	4.52	13.6	39.2	52.3			145	47,000	27
	12:00P	43.5				36.9			180	97,000	25
	2:30P	46	3.21	9.8	27.3	42.3			175	77,000	26
	4:45P	48	3.47	10.7	29.4	50.7			180	65,000	28
	6:45P	50	3.55	10.8	29.9	47.9			200	59,000	26
	9:00P	52	3.77	11.5	31.5	61.9			195	44,000	26
	10:30 P.M. TAH Removed and ECMO Discontinued: Patient Underwent Cardiac Transplantion.										

* Reptilase: Assay for determining coagulation profile during anticoagulation with heparin.

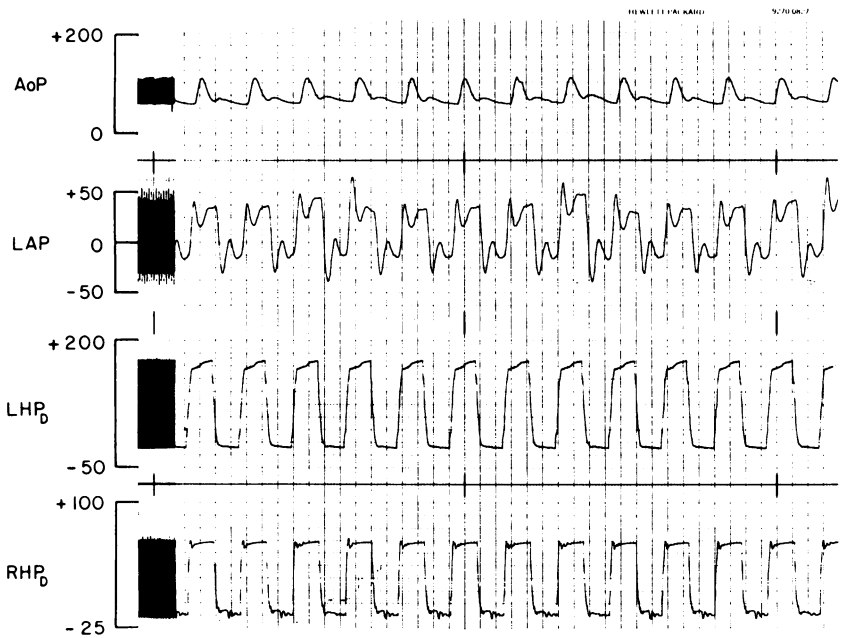

Fig. 3 Hemodynamic tracing obtained 18 hours following the total artificial heart (TAH) implantation. The aortic pressure (AoP), which was generated by the TAH was 110/65 mm Hg, with a mean of 80 mm Hg and a left heart filling pressure (left atrial pressure [LAP]) of 10 mm Hg. Left and right heart drive pressures were 160/-15 mm Hg and 60/-11 mm Hg, respectively. The patient's life was sustained by the device for approximately 54 hours, until cardiac transplantation was undertaken. Cardiac output during the entire period averaged 4.5 L/min. No deleterious hematologic effects were observed; plasma hemoglobin had decreased to 14 mg% by the eighteenth hour of TAH support.

a 4½ square meter Sci-Med Kolobow Membrane Lung. A veno-venous system was utilized and venous return was obtained from the lower inferior vena cava and both lower extremities. Return of oxygenated blood was via a long cannula inserted in the left femoral vein and advanced to the inlet of the right ventricular component of the TAH via the inferior vena cava (Fig. 4). Adequate flows were obtained (approximately 4½ L/min) by using this four-cannula approach. Increased oxygenation was achieved with oxygen saturations greater than 90% and arterial pO_2 levels ranging between 60 and 70 mm Hg. During ECMO, the $F10_2$ was reduced to 50%.

Cardiac Transplantation

The search for a donor was instituted immediately following TAH implantation. Several donors were evaluated with the aid of the Southeast-

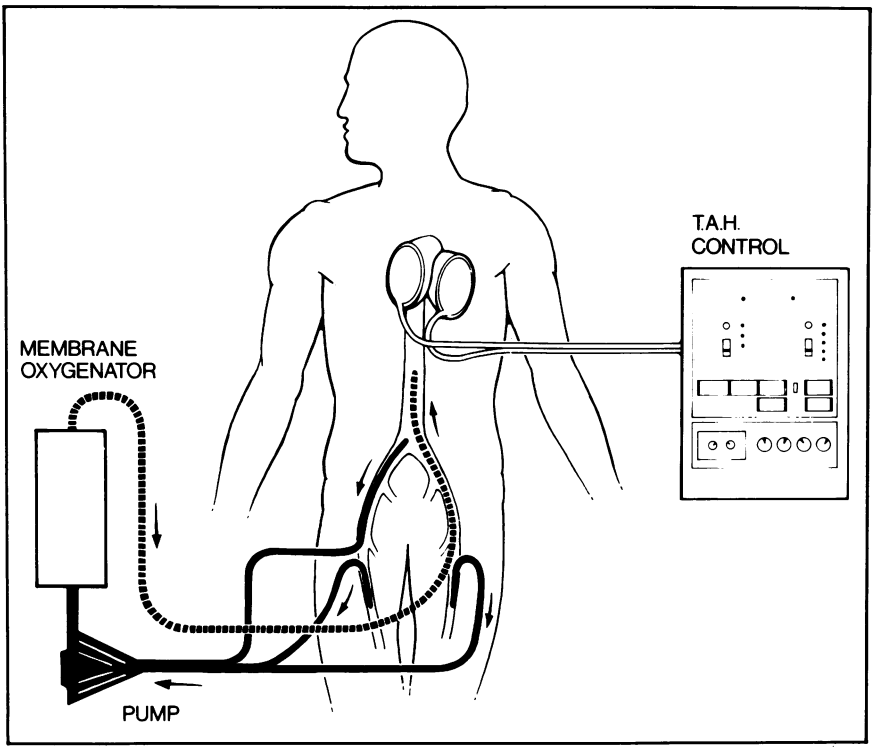

Fig. 4 Diagram of the total artificial heart and extracorporeal membrane oxygenator circuits (ECMO).

ern Organ Procurement Foundation (SEOPF).* A donor was located in another state and, along with his life-support systems, was transported to our institution by chartered jet aircraft. The donor was O RH^- HLA-AW24, ±A32; BW35, BW62, CW3, CW4. The recipient, who was supported with the total artificial heart, was A Rh^+; HLA-A3, AW24; BW44, BW39; CW5.

The donor and recipient were moved to adjacent operating rooms. The ECMO withdrawal and infusion lines were removed from the recipient. Total CPB was reinstituted by using the previous cannulation sites.The TAH was removed, leaving a cuff of woven Dacron tube on the ascending aorta and main pulmonary artery, and cardiac transplantation was effected. The allograft assumed total circulatory support at 12:24 AM on July 25 (Fig. 5).

*Richmond, Virginia (804) 353-7333

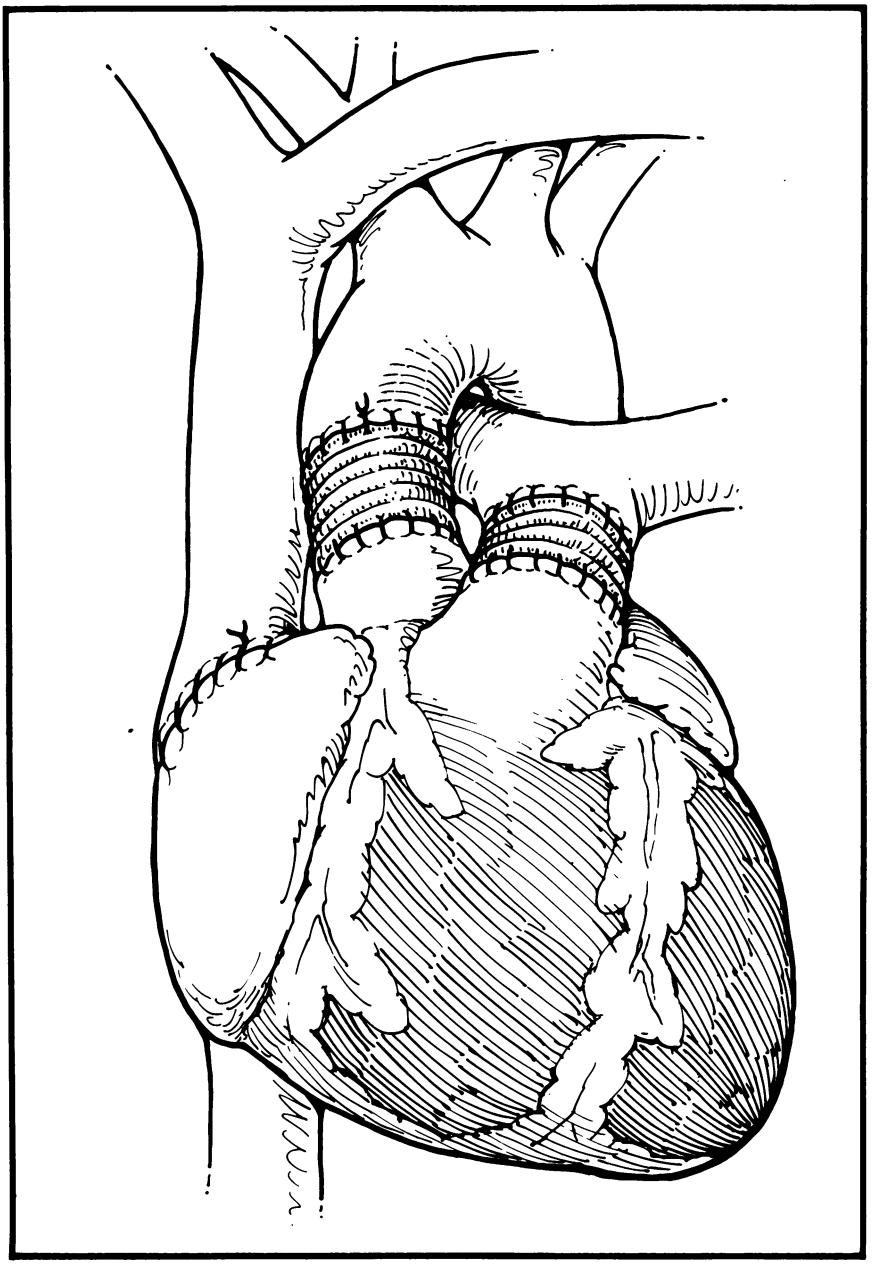

Fig. 5 Drawing of transplanted human heart in man.

Clinical Course

Coagulopathy again became a problem, but was controlled after 12 hours of intensive replacement of blood elements (Table II). Cardiac output and circulatory support were maintained satisfactorily by the allograft after initial pharmacologic treatment with Digoxin, $CaCl_2$ injections, Dobutamine, Isuprel, and Dopamine.

Immunosuppressive medication included prednisone, azathioprine (Imuran), and equine antithymocyteglobulin (ATG). Because of the known effect of ATG on platelets, it was only started 36 hours later, after the coagulopathy had abated.

Seven days after cardiac allografting, multiple organ failure was evident. Positive blood cultures for a gram negative rod and wound cultures for yeast (Candida) were reported. Thereafter, cardiac function diminished gradually and continuously despite intensive antimicrobial medication and cardiac inotropes. Cardiac action ceased at 8:00 AM on August 2, 1981.

The Prosthesis (Fig. 6)

After removal of the TAH on July 24, 1981, it was carefully examined, and no failure of materials was evident. The internal surfaces were smooth and glistening, and no thrombi had formed.

Fig. 6 Photograph showing the total artificial heart before sterilization and implantation. After removal, there was no evidence of structural failure and the internal surfaces were devoid of thrombi or neointima.

Comment

The hemodynamic function of the TAH during the 55-hour period was satisfactory, and the device maintained a relatively stable circulatory status. A pulmonary complication occurred, which was considered to be caused by a mechanical obstruction of the left pulmonary vein and possibly the right main pulmonary artery. This observation made necessary the use of the extracorporeal oxygenator (ECMO) to maintain adequate oxygenation of the blood. Also, this precipitated an urgency to proceed with cardiac transplantation. The donor heart that was finally obtained was possibly not as satisfactory from a tissue matching standpoint as would have otherwise been possible. Moreover, the allograft, although apparently free of myocardial and valve damage, appeared to be somewhat enlarged. One of the donor's kidneys and the corneas were subsequently transplanted into other recipients without reported complications.

A gratifying feature of this second clinical application of a two-staged cardiac transplantation was the absence of hemolysis caused by the TAH. In the previously reported case, in which a fabric-lined ventricle was used, the initial hemolysis was extreme, rising to 300 mg%.[4] During the 64-hour period before cardiac transplantation was performed in that case, the fabric became coated with fibrin and early neointima, and the plasma hemoglobin fell to 32 mg%. In the present case, the plasma hemoglobin was never increased by the TAH (Table II). Before TAH implantation, plasma hemoglobin was increased following 105 minutes of cardiopulmonary bypass for performance of a triple aortocoronary bypass, and insertion of the intraaortic balloon pump. After implantation of the total artificial heart, the plasma hemoglobin concentrations steadily decreased, and, 54 hours later, remained within acceptable ranges.

Acknowledgments

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References

1. Barnard CN: A human cardiac transplant: An interim report of a successful operation performed at Groote Schuur Hospital, Capetown. South African MJ 41:1271, 1967
2. Shumway NE, Stinson EB, Dong E Jr: Cardiac homotransplantation in man. Transplant Proc 1(2): 739, 1969

3. Cooley DA, Bloodwell RD, Hallman GL, Nora JJ: Transplantation of the human heart: Report of four cases. JAMA 205:479, 1968
4. Cooley DA, Liotta D, Hallman GL, Bloodwell RD, Leachman RD, Milam JD: Orthotopic cardiac prosthesis for two-staged cardiac replacement. Am J. Cardiol 24:723, 1969
5. Norman JC: An intracorporeal (abdominal) left ventricular assist device (ALVAD), XXX: Clinical readiness and initial trials in man. Cardiovascular Diseases, Bulletin of the Texas Heart Institute 3(3):249, 1976
6. Norman JC, Cooley DA, Kahan BD, Keats AS, Massin EK, Solis RT, Luper WE, Brook MI, Klima T, Frazier OH, Hacker J, Duncan JM, Dacso CC, Winston DS, Reul GJ: Total support of the circulation of a patient with post-cardiotomy stone-heart syndrome by a partial artificial heart (ALVAD) for 5 days followed by heart and kidney transplantation. Lancet 1:1125, 1978
7. McGee MG, Zillgitt SL, Trono R, Turner SA, Davis GL, Fuqua JM, Edelman SK, Norman JC: Retrospective analyses of the need for mechanical circulatory support (intraaortic balloon pump/abdominal left ventricular assist device or partial artificial heart) following cardiopulmonary bypass: A 44-month study of 14,168 patients. Am J Cardiol 46:135, 1980
8. Akutsu T: *Artificial Heart: Total Replacement and Partial Support*. Igaku Shoin, Ltd., Tokyo, 1975
9. Cheng K, Meador JW, Serrato MA, Akutsu T: The design and fabrication of a new total artificial heart. Cardiovascular Diseases, Bulletin of the Texas Heart Institute 4(1):7, 1977
10. Cooley DA, Romagnoli A, Milam JD, Bossart MI: A method of preparing woven Dacron aortic grafts to prevent interstitial hemorrhage. Cardiovascular Diseases, Bulletin of the Texas Heart Institute 8(1):48, 1981
11. Sturm JT, McGee MG, Fuhrman TM, Davis GL, Turner SA, Edelman SK, Norman JC: Treatment of postoperative low output syndrome with intraaortic balloon pumping: Experience with 419 patients. Am J Cardiol 45:1033, 1980
12. Ott DA, Cooley DA, Norman JC, Sandiford FM: Delayed sternal closure: A useful technique to prevent tamponade or compression of the heart. Cardiovascular Diseases, Bulletin of the Texas Heart Institute 5(1):15, 1978